



Claims

5

A method of treating patient who is suffering from 1. a disease, disorder or condition characterized by a bone cartilage or lung defect comprising the steps of:

- 51 -

- a) obtaining a bone marrow sample from a donor who suffering from a disease, disorder or condition characterized by a bone, cartilage or lung defect and who is syngeneic with said patient;
 - b) isolating stromal cells from said sample; and,
- c) administering said isolated stromal cells by 10 intravenous infusion to said patient.
 - The method of claim 1 wherein said patent undergoes bone marrow ablation prior to administration of isolated stromal cells.
- 15 The method of claim 2 wherein said stromal cells are 3. administered by intravenous infusion to said patient together with hematopoeitic precursor cells from a bone marrow sample from a donor who is not suffering from a disease, disorder or condition characterized by a cartilage or lung defect and who is syngeneic with said #atient. 20
 - The method of claim 2 wherein said stromal cells are administered by intravenous infusion to said patient free from hematopoeitic precursor cells.
- The method of claim 1 wherein prior to administering said stromal cells, said stromal cells are transfected with a gene construct that comprises a herpes thymidine kinase gene, wherein said gene is operably linked to regulatory sequences and is expressed by said stromal cells.
- The method of claim 1 wherein said disease, disorder or condition is characterized by a defect in said patient's 30 bone.





- 7. The method of claim of wherein said disease, disorder or condition is osteogenesis imperfecta or osteoporosis.
- 8. The method of claim 1 wherein said disease, disorder or condition is characterized by a defect in said patient's cartilage.
 - 9. The method of claim & wherein said disease, disorder or condition is chondrodysplasia or osteoarthritis.
- 10. The method of claim 1 wherein said disease, disorder or condition is characterized by defect in said patient's lungs.
 - 11. The method of claim TO wherein said disease, disorder or condition characterized is cystic fibrosis.
- 12. A method of treating patient who suffering from a disease, disorder or condition characterized by a mutated, non15 functioning or under-expressed gene which results in a defect in the bone, cartilage or lungs of said patient comprising the steps of:
 - a) obtaining a bone marrow sample from said patient;
 - b) isolating stromal cells from said sample;
- c) transfecting said stromal cells with a normal copy of said mutated, non-functioning or under-expressed gene wherein said copy of said gene is operably linked to functional regulatory elements; and
- d) administering said transfected stromal cells to 25 said patient by intravenous infusion.
 - 13. The method of claim 12 wherein said patent undergoes bone marrow ablation prior to administration of stromal cells.
 - 14. The method of claim 13 wherein said stromal cells are administered by intravenous infusion to said patient together with hematopoietic precursor cells from said sample.





15. The method of claim 12 wherein prior to administering said stromal cells, said stromal cells are transfected with a gene construct that comprises a herpes thymidine kinase gene, wherein said gene is operably linked to regulatory sequences

- 53 -

- 5 and is expressed by said stromal cells.
 - 16. The method of claim 12 wherein said disease, disorder or condition is characterized by a defect in said patient's bone.
- 17. The method of claim 16 wherein said disease, disorder or condition is osteogenesis imperfecta and said gene encodes type I procollagen or type I collagen.
 - 18. The method of claim 12 wherein said disease, disorder or condition is characterized by a defect in said patient's cartilage.
- 15 19. The method of claim 18 wherein said disease, disorder or condition is chondrodysplasia and said gene encodes type II procollagen or type II collagen.
- 20. The method of claim 12 wherein said disease, disorder or condition is characterized by defect in said patient's lungs.
 - 21. The method of claim 20 wherein said disease, disorder or condition characterized is cystic fibrosis and said gene is a cystic fibrosis gene.
 - 22. An implant device comprising:
- a container having at least one membrane surface stromal cells that comprise a gene construct, said gene construct comprising a nucleotide sequence that encodes a beneficial protein operably linked to regulatory elements which function in said stromal cell.





- 55 -

comprises said stromal cells and a container having at least one membrane surface.

- 32. The method of claim 31 wherein said membrane of said implant device has a pore size of .3 microns.
 - 33. The method of claim 21 wherein said implant device has a membrane surface area of at least 100 mm².
 - 34. The method of claim 31 wherein said implant device comprises 10^4 to 10^{11} stromal cells.
- 10 35. The method of claim 31 wherein said implant device comprises 104 to 108 stromal cells.
 - 36. The method of claim 31 wherein said implant device is implanted into said individual subcutaneously.
- 37. Immunologically isolated stromal cells that comprise a gene construct, said gene construct comprising a nucleotide sequence that encodes a beneficial protein operably linked to regulatory elements which function in said stromal cell.
 - 38. The immunologically isolated stromal cells of claim wherein said stromal cells are microencapsulated.
- 20 39. A method of treating patient who is suffering from a disease, disorder or condition characterized by a bone cartilage or lung defect comprising the steps of:
 - a) obtaining a bone marrow sample from a donor who is not suffering from a disease, disorder or condition
 25 characterized by a bone or cartilage defect and who is syngeneic with said patient; and,
 - b) administering a therapeutically effective amount of said bone marrow by intravenous infusion to said patient.





- 23. The implant device of claim 22 wherein said membrane has a pore size of .3 microns.
- 24. The implant device of claim 22 having a membrane surface area of at least 100 mm².
- 5 25. The implant device of claim 22 comprising 10° to 10¹¹ stromal cells.
 - 26. The implant device of claim 22 comprising 10^4 to 10^8 stromal cells.
- 27. The implant device of claim 22 wherein said 10 beneficial protein is selected form the group consisting of human growth hormone, obesity factor and human Factor VIII.
- 28. A method of treating an individual with a disease, disorder or condition which can be treated with a beneficial protein comprising the step of introducing into such an individual, immunologically isolated stromal cells that comprise a gene construct, said gene construct comprising a nucleotide sequence that encodes a beneficial protein operably linked to regulatory elements which function in said stromal cell.
- 20 29. The method of claim 28 wherein said disease, disorder or condition which can be treated with a beneficial protein is a disease, disorder or conditions characterized by a gene defect.
- 30. The method of claim 29 wherein said beneficial protein is selected from the group consisting of human growth hormone and human Factor VIII.
 - The method of claim 28 wherein said immunologically isolated stromal cells are within an implant device that

20



- 56 -

- 40. The method of claim 39 wherein said patent undergoes bone marrow ablation prior to administration of isolated stromal cells.
- The method of claim 39 wherein said disease, disorder or condition is characterized by a defect in said patient's bone.
 - The method of claim 41 wherein said disease, disorder or condition is osteogenesis imperfecta.
- 43. The method of claim 39 wherein said disease, disorder or condition is characterized by a defect in said patient's cartilage.
 - The method of claim 43 wherein said disease, disorder or condition is chondrodysplasia.
- 45. A method of treating patient who suffering from a disease, disorder or condition characterized by a mutated, non-functioning or under-expressed gene which results in a defect in the bone, cartilage or lungs of said patient comprising the steps of:
 - a) obtaining a bone marrow sample from said patient;
 - b) isolating stromal cells from said sample;
 - c) culturing said stromal cells under conditions which result in replication of said stromal cells into an expanded culture of stromal cells; and
- d) administering stromal cells of said expanded 25 culture of stromal cells to said patient by intravenous infusion.
 - The method of claim 45 wherein said patent undergoes bone marrow ablation prior to administration of stromal cells.





- 57 -

- 47. The method of claim 46 wherein said stromal cells are administered by intravenous infusion to said patient together with hematopoietic precursor cells from said sample.
- 48. The method of claim 46 wherein said stromal cells are administered by intravenous infusion to said patient free from precursor cells from said sample.
 - The method of claim 45 wherein said disease, disorder or condition is characterized by a defect in said patient's bone.
- 10 50. The method of claim 49 wherein said disease, disorder or condition is osteogenesis imperfecta or osteoporosis.
 - The method of claim 45 wherein said disease, disorder or condition is characterized by a defect in said patient's cartilage.
- 15 52. The method of claim 46 wherein said disease, disorder or condition is chondrodysplasia or osteoarthritis.
 - 53. The method of claim 45 wherein said disease, disorder or condition is characterized by defect in said patient's lungs.
- 20 54. The method of claim 83 wherein said disease, disorder or condition characterized is cystic fibrosis and said gene is a cystic fibrosis gene.



